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Red Cell Distribution Width as a Prognostic Marker in Severe Sepsis and Septic Shock in a Tertiary Care Centre: A Cross-Sectional Study

1. Dr. Chethan N
Postgraduate Student
Department of General Medicine
Sapthagiri Institute of Medical Sciences and Research Centre, Bengaluru, India

2.Dr Manoj B Y

Postgraduate Student

Department of General Medicine

Sapthagiri Institute of Medical Sciences and Research Centre, Bengaluru, India

3. Dr.Madhusudan C

MBBS, MD
Professor
Department of General Medicine
Sapthagiri Institute of Medical Sciences and Research Centre, Bengaluru, India

STRUCTURED ABSTRACT

Background: Sepsis is a major cause of ICU mortality. Prognostic scores like SOFA and APACHE II are complex and resource-intensive. Red Cell Distribution Width (RDW), a routinely measured and cost-effective hematologic parameter, may serve as a viable prognostic marker.

Objective: To assess RDW's prognostic value in predicting mortality and organ dysfunction in sepsis, and its correlation with clinical severity scores.

Methods: In this prospective observational study, adult sepsis patients had RDW measured on days 1 and 3. Outcomes included mortality, ICU stay, and organ dysfunction. Severity scores (SOFA, APACHE II, SIRS) and lab markers were analyzed using multivariate logistic regression, ROC curves, and correlation tests.

Results: Mortality was 67%. Non-survivors had significantly higher RDW (19.67 ± 2.73) versus survivors (13.25 ± 0.73, $p<0.001$). RDW correlated with SOFA (r=0.524), APACHE II (r=0.452), and SIRS (r=0.244). RDW >17.3% was significantly linked to acute kidney injury ($p=0.012$), liver injury ($p=0.001$), and encephalopathy ($p=0.001$). ROC analysis showed excellent diagnostic accuracy (AUC=0.95), with 72.9% sensitivity and 95.8% specificity. Integrating RDW improved existing prognostic models.

Conclusion: RDW is a reliable, economical biomarker for sepsis prognosis, correlating with illness severity and organ failure. Its inclusion in prognostic tools could enhance early risk assessment, especially in resource-constrained settings. Further multicenter validation is recommended.

Keywords: *Sepsis, RDW, Red Cell Distribution Width, Mortality, SOFA, APACHE II, Prognostic Biomarker, ICU, Inflammation, Risk Stratification*

INTRODUCTION

The Third International Consensus Definitions Task Force (SEPSIS 3) defines sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection [1], remains a major global health challenge with high morbidity and mortality [2]. Its incidence varies widely, from 103 to 240 per 100,000 people annually [3–5], with mortality rates ranging from 20–40%, reaching up to 80% in septic shock [6]. The SOFA score is widely used for assessing organ dysfunction, evaluating six organ systems based on objective parameters [7], with a score ≥2 indicating sepsis [6]. SOFA has proven reliable in predicting mortality, as validated by Vincent and Moreno et al. [8–10].

Early diagnosis and risk stratification are crucial to improve outcomes, prompting the need for accessible and reliable biomarkers [11–13]. While markers like CRP [13] and CD antigens [14] have been studied, limitations in cost and specificity restrict their utility. Red Cell Distribution Width (RDW), a standard hematological parameter reflecting erythrocyte size variability, has gained interest as a prognostic marker in sepsis. Elevated RDW results from inflammation, oxidative stress, and bone marrow suppression, contributing to the release of immature, larger RBCs [15,16].

Several studies have highlighted RDW's prognostic value. A meta-analysis by Moreno-Torres et al. linked elevated RDW at admission with increased mortality [17]. Ghimire et al. reported RDW's predictive ability comparable to SOFA and APACHE II [18]. Wang and Hsu found RDW and lactate equally effective in outcome prediction [19], while Krishna et al. showed RDW could identify high-risk septic patients [20]. Sadaka et al. demonstrated RDW's predictive superiority over SOFA and APACHE II when used alone or combined [21], and Mahmood et al. found RDW correlating with illness severity and inflammation [22]. Given this evidence, the present study aims to evaluate RDW as a prognostic marker in severe sepsis and septic shock and examine its correlation with clinical severity scores and organ dysfunction.

MATERIALS AND METHODS

This cross-sectional study was conducted over 18 months (May 2023 to November 2024) at the medical ICUs of the Department of General Medicine, Sapthagiri Institute of Medical Sciences and Research Centre, Bengaluru. The study population comprised adult patients diagnosed with severe sepsis or septic shock. Participants were selected using a simple random sampling method. Inclusion criteria were age above 18 years, meeting clinical criteria for severe sepsis or septic shock, and provision of informed written consent. Exclusion criteria included patients with pre-existing hematological disorders, history of significant blood loss (>10% of total blood volume), blood transfusion within the previous week, use of medications affecting RBC morphology, and pregnancy. The sample size was calculated using the formula $n = 4pq/d^2$, based on a prevalence of severe sepsis at 51.5%, yielding a minimum required sample of 100 participants with a 10% allowable error for statistical precision.

Following institutional ethical committee approval, eligible patients were enrolled after obtaining informed consent. Detailed history, physical examination, and

relevant investigations were recorded. Sepsis diagnosis and severity assessments were made using qSOFA, SOFA, APACHE II, and SIRS criteria at admission. Laboratory evaluations included complete hemogram with RDW and peripheral smear, measured at admission and after 72 hours. Based on RDW levels at admission, patients were stratified into three groups: Grade 1 (≤14.5), Grade 2 (14.6–17.3), and Grade 3 (>17.3). Outcomes were categorized into survivors (patients discharged after recovery) and non-survivors (patients who died during hospitalization). Clinical parameters, laboratory values, and RDW were compared between survivor and non-survivor groups.

Data were compiled using Microsoft Excel and analyzed using SPSS version 26.0. Quantitative variables were summarized using mean ± standard deviation, while qualitative variables were expressed as frequencies and proportions. ANOVA and chi-square tests were employed to assess differences among groups. Correlations were evaluated using Pearson or Spearman techniques. A p-value of <0.05 was considered statistically significant.

RESULTS

The study cohort predominantly comprised patients aged 41–60 years (38%), followed by those aged 61–80 years (34%), with fewer in the 20–40 (13%) and >80 (15%) age groups. There was a male predominance, with 60% male and 40% female participants. Regarding comorbidities, 39% had no chronic illnesses. Hypertension was the most prevalent condition (49%), followed by type 2 diabetes (29%). Bronchial asthma and chronic kidney disease each affected 5%, while ischemic heart disease and cerebrovascular accidents were seen in 3% each. Other less common comorbidities accounted for 12%. In terms of lifestyle factors, 30% reported alcohol use and 25% were smokers (Table 1).

The study cohort demonstrated notable hematologic abnormalities, with mean hemoglobin levels indicating anemia and elevated leukocyte counts on both Day 1 and Day 3 suggestive of persistent inflammation. Thrombocytopenia was present in 45% of patients, while 94% showed neutrophilic leukocytosis and 77% had normocytic normochromic anemia. Biochemical analyses revealed multi-organ involvement: elevated creatinine and bilirubin levels indicated renal and hepatic dysfunction, while markedly raised transaminases (particularly SGOT) suggested hepatocellular injury. Hypoalbuminemia was observed, aligning with catabolic stress. Vital sign monitoring revealed systemic derangement, including tachycardia, hypotension, and increased respiratory rate. Arterial blood gas analysis confirmed metabolic acidosis, reflected by a low pH, elevated lactate, and reduced bicarbonate, indicative of tissue hypoperfusion and systemic inflammatory response. Clinically, pallor was present in 44% of patients, icterus in 12%, and cyanosis and pedal edema were infrequent. Lymphadenopathy was noted in 16% (Table 2).

Blood cultures were positive in 66% of cases, with coagulase-negative staphylococci (CONS) being the most common isolate (39%), followed by E. coli, M. morganii, Klebsiella, and Pseudomonas. Urine cultures were positive in 63%, predominantly for Candida species (40%).

The mean GCS score was 8.37, reflecting considerable neurologic impairment among patients. Inflammatory and sepsis markers showed marked elevation in the study group. The mean CRP level was 110.10 mg/L, consistent with significant

systemic inflammation. Severity assessment scores revealed a mean SIRS of 2.54, APACHE II score of 37.17, and SOFA score of 12.56, indicating a high burden of physiological derangement and organ dysfunction. RDW levels were elevated (mean 17.62%) (Table 3). Grading of RDW revealed that more than half the patients (51%) had grade III RDW elevation, suggesting high variability in red blood cell size distribution (Figure 3).

Respiratory system involvement was the most common (59%) among septic patients, followed by renal (22%) and abdominal systems (13%). Skin and CNS involvement were rare. Complications included shock in all patients (100%), with acute kidney injury and liver injury affecting 55% and 44% respectively. Encephalopathy occurred in 64%, while hypoglycemia was present in 14%. ICU-related parameters showed that patients required an average of 2.17 inotropes, and the mean ICU stay was 4.21 days. Overall mortality was high, with 67% of patients succumbing to sepsis, while 33% were discharged post-recovery (Table 4).

Red Cell Distribution Width (RDW) exhibited significant positive correlations with sepsis severity indices, including SIRS ($r=0.244$), APACHE II ($r=0.452$), and SOFA score ($r=0.524$), all with statistically significant p-values, underscoring its prognostic relevance. Further, RDW levels on Day 1 were markedly elevated in non-survivors (mean 19.67) compared to survivors (mean 13.25), with a highly significant ANOVA result ($F=169.886$, $p<0.001$). Stratification by RDW grades further revealed a clear mortality gradient: 6.25% in RDW I (≤14.5%), 94.11% in RDW II (14.6–17.3%), and 96.07% in RDW III (>17.3%), with $p<0.001$. These findings highlight RDW as a robust and easily accessible marker for early identification of patients at higher risk of mortality in sepsis, supporting its inclusion in severity scoring systems (Table 5).

A statistically significant association was observed between elevated RDW grades and the incidence of sepsis-related complications. Acute kidney injury and liver injury were increasingly prevalent with rising RDW levels, with RDW III patients showing the highest incidence (65.5% and 61.4%, respectively; $p=0.012$ and $p=0.001$). Similarly, encephalopathy was most frequent in RDW III (68.8%), also reaching statistical significance ($p=0.001$). While hypoglycemia appeared more common in higher RDW grades, the difference was not statistically significant ($p=0.083$). All patients experienced shock, but due to universal occurrence, comparative statistical analysis was not applicable. These findings reinforce RDW's role as a marker of systemic severity and complication burden in sepsis (Figure 4).

DISCUSSION

Sepsis remains a major cause of ICU admissions and mortality, where early risk stratification is vital for improving clinical outcomes. Among emerging biomarkers, Red Cell Distribution Width (RDW), a routine hematological parameter, shows promise as a prognostic tool. This study assessed RDW in correlation with clinical severity indices, organ dysfunction, and mortality, and compared findings with national and international literature.

Demographic and Baseline Characteristics

Most patients in our study were aged 41–60 years (38%) and 61–80 years (34%), with a male predominance (60%). Hypertension (49%) and type 2 diabetes mellitus (29%) were common comorbidities; 39% had none. These findings align with

Mahmood NA [23], who linked elevated RDW to comorbidities including anemia, liver disease, diabetes, and alcohol use. Chaurasia AK [24] found no significant age or sex differences in outcomes. Shaikh MA [25] reported 60.5% male prevalence, consistent with our data. Jain K [26] observed a younger mean age in survivors (35.7 vs. 54.9 years), with diabetes and hypertension more common in non-survivors ($p < 0.000$). Wang TH [27] described an older cohort with high rates of CKD (58.5%), hypertension (56.3%), and diabetes (47.4%). Mahmood NA [23] also found no gender correlation with RDW in neonates. Chen CK [28] reported 49% of patients were over 65 years, with higher mortality among elderly and those with comorbidities.

Vital Parameters and Blood Gas Analysis

Our patients had hypotension (SBP 82.78 mmHg), tachycardia (107 bpm), and elevated respiratory rates, along with metabolic acidosis (pH 7.22, HCO_3 15.32, lactate 3.96 mmol/L). Chaurasia AK [24] and Shaikh MA [25] both noted significantly worse vital signs in non-survivors, indicating circulatory collapse.

Systemic and Clinical Presentation

Respiratory involvement (59%) was predominant. This is comparable to Shaikh M [25], where bronchopneumonia was the leading cause of sepsis, and to Jain K [26], who observed fever and respiratory distress as common symptoms. Wang TH [27] also reported respiratory infections as the most frequent source of sepsis.

Sepsis and Severity Scores

Our patients had high CRP (110.10 mg/L), SIRS (2.54), APACHE II (37.17), and SOFA (12.56). RDW showed significant correlation with SIRS ($r=0.244$), APACHE II ($r=0.452$), and SOFA ($r=0.524$). Mahmood NA [23] found a weaker but significant RDW-APACHE II correlation ($r^2 = 0.09$). RDW ≥16% remained predictive after adjusting for confounders. Shaikh MA [25] found that higher RDW groups had elevated SOFA scores. Jain K [26] reported RDW as an independent predictor of mortality. Wang TH [27] showed significantly higher SOFA and lower hemoglobin levels in patients with high RDW.

Outcomes

Our mortality rate was 67%. Non-survivors had significantly higher RDW (19.67 vs. 13.25; $p<0.001$). Mahmood NA [23] noted increased mortality risk with RDW ≥16%. Moreno-Torres V [29] reported RDW ≥16% associated with a 70% mortality risk. Wu YC [30] found elevated RDW linked to a 1.887 hazard ratio for mortality post-PSM. Chaurasia AK [24] identified an RDW >14.35% as predictive (AUC = 0.805). Deka A [31] showed RDW's predictive accuracy in neonates even when sepsis screen was negative. Shaikh MA [25] and Jain K [26] reported significantly higher RDW in non-survivors with strong statistical association. Wang TH [27] demonstrated RDW had a predictive AUC of 0.71, outperforming lactate and nearing SOFA's accuracy. Chen CK [28] found highest mortality in the top RDW quartile (16.7%), with diagnostic odds ratio of 5.69. Liao J [32] showed RDW >15.7% predicted higher 28-day mortality and longer ICU stays.

RDW Association with Complications

AKI, liver injury, and encephalopathy increased significantly with rising RDW grades in our study. Moreno-Torres V [29] confirmed RDW's predictive

sensitivity (0.81) and specificity (0.65). Wu YC [30] found elevated RDW increased mortality risk across septic shock, mechanical ventilation, and bacteremia subgroups. Wang TH [27] reported RDW associated with higher ICU admission, shock, and mortality. Chen CK [28] correlated elevated RDW with worse biochemical parameters (e.g., creatinine, bilirubin, ammonia), supporting its role as a systemic severity marker.

Overall, our findings reaffirm the growing body of evidence that elevated RDW is not merely a nonspecific hematological abnormality, but a strong, independent predictor of disease severity and adverse outcomes in sepsis. The graded increase in mortality, organ dysfunction (renal, hepatic, neurological), and severity scores (SOFA, APACHE II, SIRS) with rising RDW levels suggests a dose-response relationship that holds both statistical and clinical significance. This, coupled with RDW's cost-effectiveness and ease of access, supports its incorporation into standard sepsis evaluation protocols. However, further multicenter studies with larger cohorts are essential to establish standardized RDW cut-offs and validate its role across diverse patient populations.

CONCLUSION

This study reinforces Red Cell Distribution Width (RDW) as a robust, independent prognostic marker in sepsis, correlating strongly with organ dysfunction, severity scores (SOFA, APACHE II, SIRS), and mortality. RDW levels above 17% were particularly associated with adverse outcomes, including a significantly higher risk of acute kidney injury, liver dysfunction, encephalopathy, and death. Compared to other studies, our results are consistent with global evidence underscoring RDW's predictive accuracy. Given its cost-effectiveness, availability, and diagnostic performance, RDW merits integration into clinical protocols for sepsis management and outcome prediction.

Table 1: Demographic characteristics and comorbidities of Study Population

Variable	Category	n (%)
Age	20–40 years	13 (13.0%)
	41–60 years	38 (38.0%)
	61–80 years	34 (34.0%)
	>80 years	15 (15.0%)
Sex	Male	60 (60.0%)
	Female	40 (40.0%)
Comorbidities	None	39 (39.0%)
	Hypertension	49 (49.0%)
	Type 2 Diabetes Mellitus	29 (29.0%)
	Bronchial Asthma	5 (5.0%)
	Chronic Kidney Disease (CKD)	5 (5.0%)
	Ischemic Heart Disease (IHD)	3 (3.0%)
	Cerebrovascular Accident (CVA)	3 (3.0%)
	Others	12 (12.0%)
Lifestyle Factors	Alcohol Use	30 (30.0%)
	Smoker	25 (25.0%)

Table 2: Clinical and Laboratory Characteristics of the Study Population

Variable	Category	n (%)
Hematological Parameters	Hemoglobin (g/dL)	10.61 ± 2.23
	Total Leukocyte Count (Day 1)	19116.38 ± 7049.56
	Total Leukocyte Count (Day 3)	23695.59 ± 11811.70
	Platelet Count (Lakhs/µL)	1.76 ± 1.14
	ESR (mm/hr)	49.93 ± 30.86
Peripheral Smear Findings	Neutrophilic Leukocytosis	94 (94.0%)
	Normocytic Normochromic	77 (77.0%)
	Thrombocytopenia	45 (45.0%)
	Dimorphic Picture	13 (13.0%)
	Microcytic Hypochromic	4 (4.0%)
	Pancytopenia	4 (4.0%)
Biochemical Parameters	Serum Creatinine (mg/dL)	2.22 ± 1.78
	Serum Bilirubin (mg/dL)	2.39 ± 3.34
	SGOT (U/L)	278.98 ± 1389.04
	SGPT (U/L)	104.51 ± 379.70
	Serum Albumin (g/dL)	2.64 ± 0.75
	Random Blood Sugar (mg/dL)	166.95 ± 113.63
Vital Signs	Pulse Rate (beats/min)	107.15 ± 17.29
	Systolic BP (mmHg)	82.78 ± 10.18
	Diastolic BP (mmHg)	55.04 ± 8.53
	Respiratory Rate (/min)	22.00 ± 4.12
ABG Parameters	pH	7.22 ± 0.15
	pCO_2 (mmHg)	37.91 ± 12.16
	pO_2 (mmHg)	64.90 ± 27.94
	Lactate (mmol/L)	3.96 ± 2.35
	HCO_3 (mmol/L)	15.32 ± 6.25
Clinical Signs	Pallor	44 (44.0%)
	Icterus	12 (12.0%)
	Cyanosis	5 (5.0%)
	Clubbing	3 (3.0%)
	Pedal Edema	7 (7.0%)
	Lymphadenopathy	16 (16.0%)

Table 3: Inflammatory and Sepsis-Related Markers in the Study Population

Parameter	Mean ± SD
C-Reactive Protein (CRP, mg/L)	110.10 ± 59.67
SIRS Score	2.54 ± 0.52
APACHE II Score	37.17 ± 13.50
SOFA Score	12.56 ± 3.71
Red Cell Distribution Width (RDW, %)	17.62 ± 3.78
Glasgow Coma Scale (GCS)	8.37 ± 4.36

Table 4: Systemic Involvement, Organ Injuries, ICU Parameters, and Patient Outcomes

Variable	Category	n (%)
System Involvement	Respiratory	59 (59.0%)
	Kidney	22 (22.0%)
	Abdomen	13 (13.0%)
	CNS	4 (4.0%)
	Skin	2 (2.0%)
Organ Injury & Complications	Acute Kidney Injury	55 (55.0%)
	Acute Liver Injury	44 (44.0%)
	Shock	100 (100.0%)
	Encephalopathy	64 (64.0%)
	Hypoglycemia	14 (14.0%)
Number of Inotropes		2.17 ± 0.85
Number of Days in ICU		4.21 ± 1.42
Outcome	Death	67 (67.0%)
	Discharged	33 (33.0%)

Table 5: Correlation and Prognostic Value of RDW in Sepsis Outcomes

Analysis Type	Variable/Group	Value	p-value
Pearson Correlation with RDW	SIRS Score	r = 0.244	0.014
	APACHE II Score	r = 0.452	0.001
	SOFA Score	r = 0.524	0.001
ANOVA – RDW by Outcome	Death	19.67 ± 2.73	< 0.001
	Discharged	13.25 ± 0.73	
Mortality by RDW Grade	RDW Grade I (≤14.5%)	6.25% mortality	< 0.001
	RDW Grade II (14.6–17.3%)	94.11% mortality	
	RDW Grade III (>17.3%)	96.07% mortality	

Figure 1. Blood culture

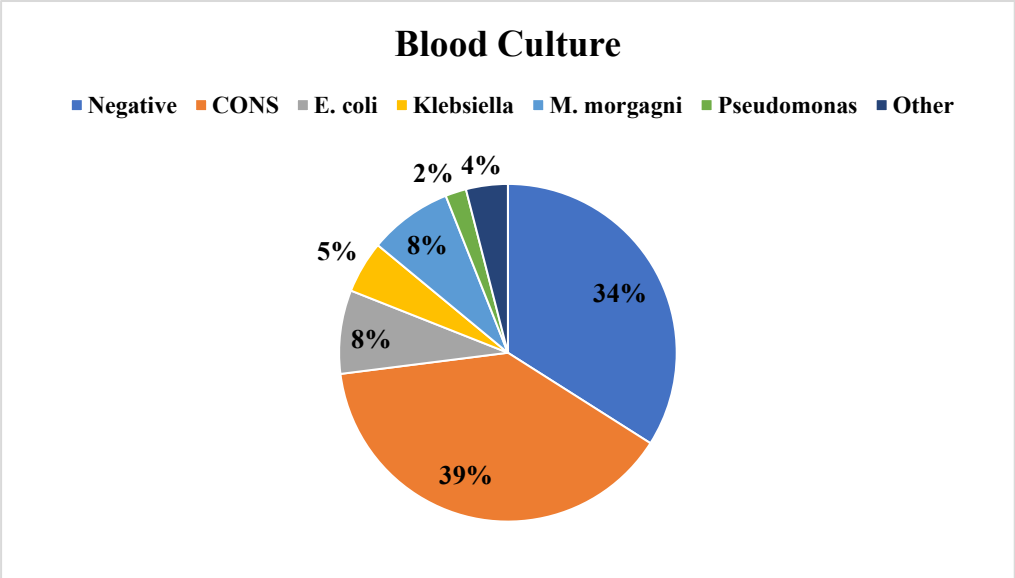


Figure 2. Urine culture

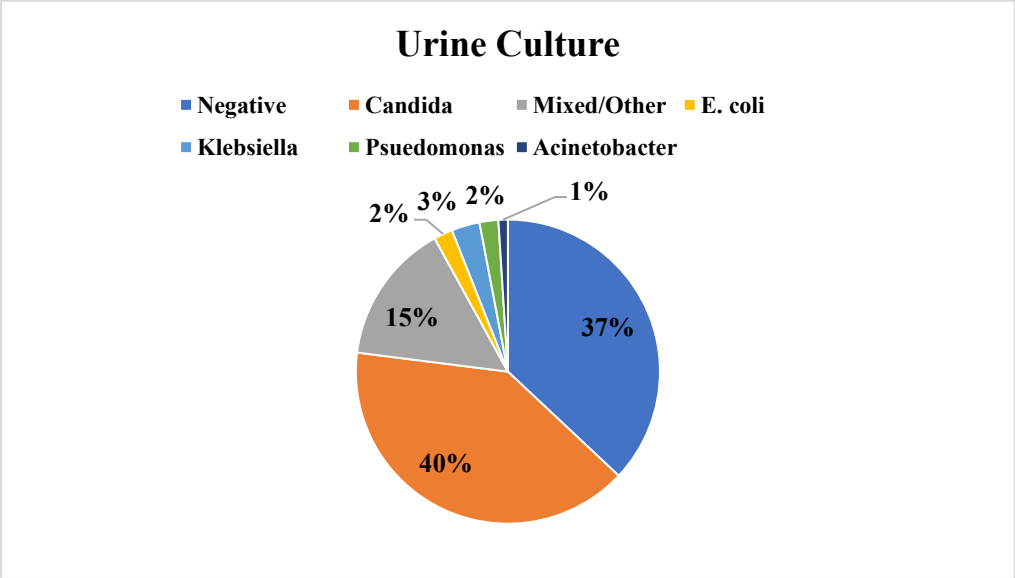


FIGURE 3. GRADING OF RDW

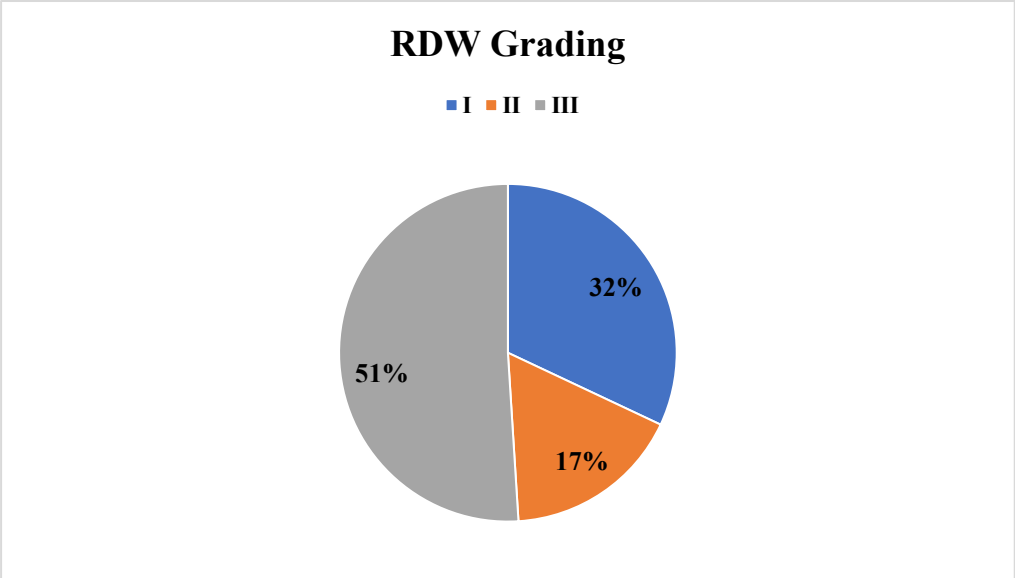
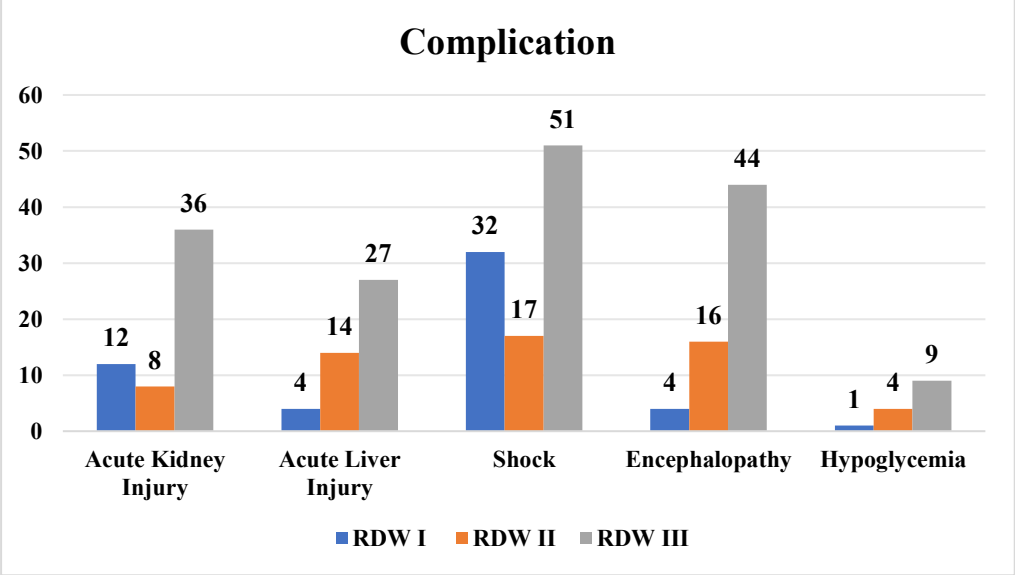


FIGURE 4. ASSOCIATION OF RDW WITH COMPLICATION



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